

In the specification:

Insert the paper copy of the Sequence Listing filed herewith following the Oath/Declaration.

Please amend the paragraph beginning at page 1, line 16, as follows:

a²
An alternate human parathyroid hormone (PTH) receptor, designated as PTH2 receptor, has been identified in rat and human brain. This receptor is selectively activated by PTH-(1-34) (SEQ ID NO:1), but not PTH-related protein PTHrP-(1-34) (SEQ ID NO:2), which has the same calcium-mobilizing activities as PTH-(1-34) (SEQ ID NO:1). Both PTH and PTHrP share a common G protein-coupled receptor, termed the PTH/PTHrP receptor. The PTH2 receptor is localized predominantly in the brain and pancreas, in contrast to PTH/PTHrP receptor, which is primarily localized in bone and the kidney, the principal target tissue for PTH action. Parathyroid hormone (PTH) is the principal physiological regulator of calcium levels in the blood (Chorev, M., Rosenblatt, M., 1994, Structure function analysis of parathyroid hormone and parathyroid hormone-related protein, Bilezikian, J.P., Marcus, R., Levine, M., (eds) The Parathyroids: Basic and Clinical Concepts. Raven Press, New York, pp 139-156; Juppner, H., et al., 1991, Science, 254:1024-1026; and Martin, T.J., et al., 1991, Crit. Rev. Biochem. Mol. Biol. 26:377-395). PTH-related protein (PTHrP) was originally identified as the agent responsible for the paraneoplastic syndrome of humoral hypercalcemia of malignancy (Suva, L.J., et al., 1987, Science, 237:893-896 and Orloff, J.J., et al., 1994, Endocrinol. Rev. 15:40-60). PTH and PTHrP are products of distinct, yet evolutionary-related genes. PTH and PTHrP show sequence similarities only in the N-terminal 13 amino acids, 8 of which are identical (Abou-Samra AB, et al., 1992, Proc. Natl. Sci. Acad. USA, 89:2732-2736). However, the expression pattern and physiological role of these two molecules are remarkably different. PTH has a highly restricted pattern of expression and acts as a classical endocrine hormone, whereas PTHrP is expressed in a wide variety of normal tissues and functions in a predominantly autocrine/paracrine fashion (Urena, P., et al., 1993, Endocrinology, 133:617-623; Lee, K., et al., 1995, Endocrinology, 136:453-463; and Martin, T.J., et al., 1995, Miner. Electrolyte Metab., 21:123-128). More

a2 recently, PTHrP has been shown to play a fundamental role in embryonic differentiation of bone and cartilage development.

Please amend the paragraph beginning at page 3, line 8, as follows:

An homologous receptor for PTH, designated the PTH2 receptor, has been identified and partially characterized (Behar, V., et al., 1996, Endocrinology, 137:2748-2757; Gardella, T.J., et al., 1996, The J. Biol. Chem., 271:19888-19893; Behar, V., et al., 1996, Endocrinology, 137:4217-4224; and Usdin, T.B., et al., 1997, Endocrinology, 138:831-834). Amongst the seven transmembrane G protein-coupled receptors, the PTH2 receptor is most similar in sequence to the PTH/PTHrP receptor (51% of the amino acid sequence identify). Interestingly, PTH2 receptor mRNA is not detected in bone or osteosarcoma cell lines, but is expressed in a number of tissues including the exocrine pancreas, lung, heart, vasculature, and epididymis, and is most abundant in the brain (Usdin, T.B., et al., 1996, Endocrinology, 137:4285-4297). Unlike the PTH/PTHrP receptor, which binds and is activated by both PTH-(1-34) (SEQ ID NO:1) and PTHrP-(1-34) (SEQ ID NO:2), the PTH2 receptor binds and is activated only by PTH-(1-34) (SEQ ID NO:1). [PTHrP (7-34)] PTHrP-(1-34) (SEQ ID NO:2) was found to recognize PTH2 receptor and weakly activate it. Moreover, His⁵ in PTHrP was identified as the "specificity switch" for the PTH2 receptor. Swapping a single amino acid, His⁵ from PTHrP, with Ile⁵ from PTH, resulted in a PTHrP analogue, Ile⁵-PTHrP-(1-34) NH₂ (SEQ ID NO:3), which acts as a PTH-2 receptor agonist. Hence, the single amino acid switch converts inactive PTHrP into a potent PTH2 receptor agonist. But while [Ile⁵] PTHrP (SEQ ID NO:3) binds and activates both receptors, PTH/PTHrP and PTH2, it is not a selective PTH2 agonist. In transient heterologous (with respect to species) expression systems, others have found an additional contribution to hPTH2 receptor selectivity by Trp²³ (Gardella et al., JBC 1996, 271:19888-19893). Like the PTH/PTHrP receptor, PTH binding leads to PTH2 receptor-mediated activation of both cAMP and [Ca²⁺] intracellular signaling pathways.

Please amend the paragraph beginning at page 5, line 8, as follows:

A more preferred PTH analogue that selectively binds to the PTH2 receptor is an analogue of formula (I), $(R^1R^2)-A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8-A^9-A^{10}-A^{11}-A^{12}-A^{13}-A^{14}-A^{15}-A^{16}-A^{17}-A^{18}-A^{19}-A^{20}-A^{21}-A^{22}-A^{23}-A^{24}-A^{25}-A^{26}-A^{27}-A^{28}-A^{29}-A^{30}-A^{31}-A^{32}-A^{33}-A^{34}-A^{35}-A^{36}-A^{37}-A^{38}-R^3$,

(I)

or a pharmaceutically-acceptable salt thereof wherein

A^1 is a hydrophilic or a lipophilic amino acid;

A^2 is a lipophilic amino acid;

A^3 is a hydrophilic or a lipophilic amino acid;

A^4 is a hydrophilic amino acid;

A^5 is a hydrophilic or a lipophilic amino acid;

A^6 is a hydrophilic amino acid or is deleted;

A^7 is a hydrophilic or a lipophilic amino acid or is deleted;

A^8 is a lipophilic amino acid or is deleted;

A^9 is a hydrophilic amino acid or is deleted;

A^{10} is a hydrophilic amino acid or is deleted;

A^{11} is a hydrophilic or a lipophilic amino acid or is deleted;

A^{12} is a hydrophilic or a lipophilic amino acid or is deleted;

A^{13} is a hydrophilic amino acid;

A^{14} is a hydrophilic amino acid or is deleted;

A^{15} is a lipophilic amino acid or is deleted;

A^{16} is a hydrophilic or a lipophilic amino acid or is deleted;

A^{17} is a hydrophilic or a lipophilic amino acid or is deleted;

A^{18} is a lipophilic amino acid or is deleted;

A^{19} is a hydrophilic or a lipophilic amino acid or is deleted;

A^{20} is a hydrophilic amino acid or is deleted;

A^{21} is a hydrophilic or a lipophilic amino acid or is deleted;

A^{22} is a lipophilic or a hydrophilic amino acid or is deleted;

a4

A²³ is a hydrophilic or a lipophilic amino acid;
A²⁴ is a hydrophilic or a lipophilic amino acid;
A²⁵ is a hydrophilic amino acid;
A²⁶ is a hydrophilic amino acid;
A²⁷ is a lipophilic or a hydrophilic amino acid;
A²⁸ is a lipophilic amino acid;
A²⁹ is a lipophilic or a hydrophilic amino acid;
A³⁰ is a hydrophilic or a lipophilic amino acid;
A³¹ is a lipophilic or a hydrophilic amino acid or is deleted;
A³² is a hydrophilic amino acid or is deleted;
A³³ is a hydrophilic amino acid or is deleted;
A³⁴ is a lipophilic amino acid or is deleted;
A³⁵ is a lipophilic amino acid or is deleted;
A³⁶ is a lipophilic or a hydrophilic amino acid or is deleted;
A³⁷ is a lipophilic amino acid or is deleted;
A³⁸ is a lipophilic or a hydrophilic amino acid or is deleted;

A4
cont

R¹ and R² are each independently selected from the group consisting of H, (C₁-C₃₀)alkyl, (C₂-C₃₀)alkenyl, phenyl-(C₁-C₃₀)alkyl, naphthyl(C₁-C₃₀)alkyl, hydroxy(C₁-C₃₀)alkyl, hydroxy(C₂-C₃₀)alkenyl, hydroxy-phenyl(C₁-C₃₀)alkyl or hydroxy-naphthyl(C₁-C₃₀)alkyl;
or one of R¹ or R² is COE¹ where E¹ is (C₁-C₃₀)alkyl, (C₂-C₃₀)alkenyl, phenyl(C₁-C₃₀)alkyl, naphthyl(C₁-C₃₀)alkyl, hydroxy(C₁-C₃₀)alkyl, hydroxy(C₂-C₃₀)alkenyl, hydroxy-phenyl(C₁-C₃₀)alkyl or hydroxy-naphthyl(C₁-C₃₀)alkyl; and
R³ is OH, NH₂, (C₁-C₃₀)alkoxy or NH-Y-CH₂-Z, where Y is a (C₁-C₃₀) hydrocarbon moiety and Z is CO₂H or CONH₂;

provided that the compound is not PTH(1-34)R³ (SEQ ID NO:4), PTH(1-35)R³ (SEQ ID NO:5), PTH(1-36)R³ (SEQ ID NO:6), PTH(1-37)R³ (SEQ ID NO:7), or PTH(1-38)R³ (SEQ ID NO:8).

Please amend the paragraph beginning at page 7, line 3, as follows:

Another preferred group of PTH analogues that selectively binds to the PTH2 receptor is an analogue of formula (II), $(R^1R^2)-A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8-A^9-A^{10}-A^{11}-A^{12}-A^{13}-A^{14}-A^{15}-A^{16}-A^{17}-A^{18}-A^{19}-A^{20}-A^{21}-A^{22}-A^{23}-A^{24}-A^{25}-A^{26}-A^{27}-A^{28}-A^{29}-A^{30}-A^{31}-A^{32}-A^{33}-A^{34}-A^{35}-A^{36}-A^{37}-A^{38}-R^3$,

(II)

or a pharmaceutically-acceptable salt thereof wherein

A^1 is Ser, Ala, Dap, Thr, Aib or is deleted;

A^2 is Val, Leu, Ile, Phe, Nle, β -Nal, Aib, p-X-Phe, Acc, Cha, Met or is deleted;

A^3 is Ser, Thr, Aib or is deleted;

A^4 is Glu, Asp or is deleted;

A^5 is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe or is deleted;

A^6 is Gln, a hydrophilic amino acid or is deleted;

A^7 is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe, a lipophilic amino acid, or is deleted;

A^8 is Met, Nva, Leu, Val, Ile, Cha, Acc, Nle, p-X-Phe, Phe, β -Nal, Bpa, a lipophilic amino acid or is deleted;

A^9 is His, a hydrophilic amino acid or is deleted;

A^{10} is Asn, a hydrophilic amino acid or is deleted;

A^{11} is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe, a hydrophilic amino acid or is deleted;

A^{12} is Gly, Acc, Aib, or is deleted;

A^{13} is Lys, Arg or $HN-CH((CH_2)_nNH-R^4)-C(O)$;

A^{14} is His or is deleted;

A^{15} is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe or is deleted;

A^{16} is Ser, Asn, Ala, Aib or is deleted;

A^{17} is Ser, Thr, Aib or is deleted;

A^{18} is Met, Nva, Leu, Val, Ile, Nle, p-X-Phe, Phe, β -Nal, Acc, Cha, Aib or is deleted;

A^{19} is Glu, Aib or is deleted;

A²⁰ is Arg, Lys, HN-CH((CH₂)_nNH-R⁴)-C(O) or is deleted;

A²¹ is Val, Leu, Ile, Phe, Nle, β-Nal, Aib, p-X-Phe, Acc, Cha, Met or is deleted;

A²² is Acc, Aib, Glu or is deleted;

A²³ is Trp, Acc, Phe, p-X-Phe, Aib, β-Nal or Cha;

A²⁴ is Leu, Acc, Ile, Val, Phe, β-Nal, Nle, Aib, p-X-Phe or Cha;

A²⁵ is Arg, Lys or HN-CH((CH₂)_nNH-R⁴)-C(O);

A²⁶ is Arg, Lys or HN-CH((CH₂)_nNH-R⁴)-C(O);

A²⁷ is Lys, Aib, Leu, hArg, Gln, Acc, Arg, Cha, Nle, Ile, Val, Phe, β-Nal, or p-X-Phe, where the Lys is optionally substituted on the ε-amino group by an acyl group;

A²⁸ is Leu, Acc, Cha, Ile, Val, Phe, Nle, β-Nal, Aib or p-X-Phe;

A²⁹ is Gln, Acc or Aib;

A³⁰ is Asp, Lys, Arg or is deleted;

A³¹ is Val, Leu, Nle, Acc, Cha, Phe, Ile, β-Nal, Aib, p-X-Phe or is deleted;

A³² is His or is deleted;

A³³ is Asn or is deleted;

A³⁴ is Phe, Tyr, Amp, Aib, β-Nal, Cha, Nle, Leu, Ile, Acc, p-X-Phe or is deleted;

A³⁵ is Val, Leu, Nle, Acc, Cha, Phe, Ile, β-Nal, Aib, p-X-Phe or is deleted;

A³⁶ is Ala, Val, Aib, Acc, Nva, Abu or is deleted;

A³⁷ is Leu, Val, Nle, Ile, Cha, β-Nal, Trp, Pal, Acc, Phe, p-X-Phe, a lipophilic amino acid, or is deleted;

A³⁸ is Gly, Acc, Aib, or is deleted;

where X for each occurrence is independently selected from the group consisting of OH, a halo and CH₃;

R¹ and R² are each independently selected from the group consisting of H, (C₁-C₃₀)alkyl, (C₂-C₃₀)alkenyl, phenyl-(C₁-C₃₀)alkyl, naphthyl(C₁-C₃₀)alkyl, hydroxy(C₁-C₃₀)alkyl, hydroxy(C₂-C₃₀)alkenyl, hydroxy-phenyl(C₁-C₃₀)alkyl or hydroxy-naphthyl(C₁-C₃₀)alkyl;

as
cont

or one of R¹ or R² is COE¹ where E¹ is (C₁-C₃₀)alkyl, (C₂-C₃₀)alkenyl, phenyl(C₁-C₃₀)alkyl, naphthyl(C₁-C₃₀)alkyl, hydroxy(C₁-C₃₀)alkyl, hydroxy(C₂-C₃₀)alkenyl, hydroxy-phenyl(C₁-C₃₀)alkyl or hydroxy-naphthyl(C₁-C₃₀)alkyl;

R³ is OH, NH₂, (C₁-C₃₀)alkoxy or NH-Y-CH₂-Z, where Y is a (C₁-C₃₀) hydrocarbon moiety and Z is CO₂H or CONH₂;

n for each occurrence is independently an integer from 1 to 5; and

R⁴ for each occurrence is independently (C₁-C₃₀)alkyl, (C₁-C₃₀)acyl or -C((NH)(NH₂));

provided that the compound is not PTH(1-34)R³ (SEQ ID NO:4), PTH(1-35)R³ (SEQ ID NO:5), PTH(1-36)R³ (SEQ ID NO:6), PTH(1-37)R³ (SEQ ID NO:7), or PTH(1-38)R³ (SEQ ID NO:8).

Please amend the paragraph beginning at page 9, line 11, as follows:

In another respect, this invention provides a PTHrP analogue that selectively binds to the PTH2 receptor of the formula (IV), (R¹R²)-A¹-A²-A³-A⁴-A⁵-A⁶-A⁷-A⁸-A⁹-A¹⁰-A¹¹-A¹²-A¹³-A¹⁴-A¹⁵-A¹⁶-A¹⁷-A¹⁸-A¹⁹-A²⁰-A²¹-A²²-A²³-A²⁴-A²⁵-A²⁶-A²⁷-A²⁸-A²⁹-A³⁰-A³¹-A³²-A³³-A³⁴-A³⁵-A³⁶-A³⁷-A³⁸-R³,

(IV)

or a pharmaceutically acceptable salt thereof, wherein

A¹ is Ala, Ser, Dap, Thr, Aib or is deleted;

A² is Val or is deleted;

A³ is Ser, Aib, Thr or is deleted;

A⁴ is Glu, Asp or is deleted;

A⁵ is His, Ile, Acc, Val, Nle, Phe, Leu, p-X-Phe, β-Nal, Aib, Cha or is deleted;

A⁶ is Gln, a hydrophilic amino acid or is deleted;

A⁷ is Leu, Val, Cha, Nle, β-Nal, Trp, Pal, Acc, Phe, p-X-Phe, Aib, a lipophilic amino acid or is deleted;

A⁸ is Leu, Met, Acc, Cha, Aib, Nle, Phe, Ile, Val, β-Nal, p-X-Phe, a lipophilic amino acid or is deleted;

A⁹ is His, a hydrophilic amino acid or is deleted;

A¹⁰ is Asp, Asn, a hydrophilic amino acid or is deleted;

A¹¹ is Lys, Arg, Leu, Cha, Aib, p-X-Phe, Ile, Val, Nle, Acc, Phe, β -Nal, HN-CH((CH₂)_nNH-R⁴)-C(O), a lipophilic D-amino acid, a hydrophilic amino acid or is deleted;

A¹² is Gly, Acc, Aib or is deleted;

A¹³ is Lys, Arg, HN-CH((CH₂)_nNH-R⁴)-C(O) or is deleted;

A¹⁴ is Ser, His or is deleted;

A¹⁵ is Ile, Acc, Cha, Leu, Phe, Nle, β -Nal, Trp, p-X-Phe, Val, Aib or is deleted;

A¹⁶ is Gln, Aib or is deleted;

A¹⁷ is Asp, Aib or is deleted;

A¹⁸ is Leu, Aib, Acc, Cha, Phe, Ile, Nle, β -Nal, Val, p-X-Phe or is deleted;

A¹⁹ is Arg, Lys, Aib, HN-CH((CH₂)_nNH-R⁴)-C(O) or is deleted;

A²⁰ is Arg, Lys, HN-CH((CH₂)_nNH-R⁴)-C(O) or is deleted;

A²¹ is Arg, Lys, HN-CH((CH₂)_nNH-R⁴)-C(O) or is deleted;

A²² is Phe, Glu, Aib, Acc, p-X-Phe, β -Nal, Val, Leu, Ile, Nle or Cha;

A²³ is Phe, Leu, Lys, Acc, Cha, β -Nal, Aib, Nle, Ile, p-X-Phe, Val or Trp;

A²⁴ is Leu, Lys, Acc, Nle, Ile, Val, Phe, β -Nal, Aib, p-X-Phe, Arg or Cha;

A²⁵ is His, Lys, Aib, Acc, Arg or Glu;

A²⁶ is His, Aib, Acc, Arg or Lys;

A²⁷ is Leu, Lys, Acc, Arg, Ile, Val, Phe, Aib, Nle, β -Nal, p-X-Phe or Cha;

A²⁸ is Ile, Leu, Lys, Acc, Cha, Val, Phe, p-X-Phe, Nle, β -Nal, Aib or is deleted;

A²⁹ is Ala, Glu, Acc, Aib or is deleted;

A³⁰ is Glu, Leu, Nle, Cha, Aib, Acc, Lys, Arg or is deleted;

A³¹ is Ile, Leu, Cha, Lys, Acc, Phe, Val, Nle, β -Nal, Arg or is deleted;

A³² is His or is deleted;

A³³ is Thr, Ser or is deleted;

A³⁴ is Ala, Phe, Tyr, Cha, Val, Ile, Leu, Nle, β -Nal, Aib, Acc or is deleted;

A³⁵ is Glu, Asp or is deleted;

A³⁶ is Ile, Acc, Cha, Leu, Phe, Nle, β -Nal, Trp, p-X-Phe, Val, Aib or is deleted;

A³⁷ is Arg, Lys, HN-CH((CH₂)_nNH-R⁴)-C(O) or is deleted;

A³⁸ is Ala, Phe, Tyr, Cha, Val, Ile, Leu, Nle, β -Nal, Aib, Acc or is deleted;

Ab
Cont

a6

R¹ and R² are each independently selected from the group consisting of H, (C₁-C₃₀)alkyl, (C₂-C₃₀)alkenyl, phenyl-(C₁-C₃₀)alkyl, naphthyl(C₁-C₃₀)alkyl, hydroxy(C₁-C₃₀)alkyl, hydroxy(C₂-C₃₀)alkenyl, hydroxy-phenyl(C₁-C₃₀)alkyl or hydroxy-naphthyl(C₁-C₃₀)alkyl;
or one of R¹ or R² is COE¹ where E¹ is (C₁-C₃₀)alkyl, (C₂-C₃₀)alkenyl, phenyl(C₁-C₃₀)alkyl, naphthyl(C₁-C₃₀)alkyl, hydroxy(C₁-C₃₀)alkyl, hydroxy(C₂-C₃₀)alkenyl, hydroxy-phenyl(C₁-C₃₀)alkyl or hydroxy-naphthyl(C₁-C₃₀)alkyl;
R³ is OH, NH₂, (C₁-C₃₀)alkoxy or NH-Y-CH₂-Z, where Y is a (C₁-C₃₀) hydrocarbon moiety and Z is CO₂H or CONH₂;
n for each occurrence is independently an integer from 1 to 5; and
R⁴ for each occurrence is independently (C₁-C₃₀)alkyl, (C₁-C₃₀)acyl or -C((NH)(NH₂));

provided that the compound is not PTHrP(1-34)R³ (SEQ ID NO:9), PTHrP(1-35)R³ (SEQ ID NO:10), PTHrP(1-36)R³ (SEQ ID NO:11), PTHrP(1-37)R³ (SEQ ID NO:12) or PTHrP(1-38)R³ (SEQ ID NO:13), and further provided that the compound is not [Ile⁵, Trp²³] PTHrP(1-36) (SEQ ID NO:14) or [Trp²³] PTHrP(1-36) (SEQ ID NO:15).

Please amend the paragraph beginning at page 14, line 9, as follows:

a7

A preferred group of compounds of formula (III) are the compounds listed as Examples 1-73, shown hereinbelow. Of the compounds listed as Examples 1-73, the following compounds are preferred: [Cha^{7,11}, des-Met⁸, Nle¹⁸, Tyr³⁴]hPTH-(1-34)NH₂ (SEQ ID NO:16), [Cha^{7,11}, D-Nle⁸, des-Met¹⁸, Tyr³⁴]hPTH-(1-34)NH₂, [Cha^{7,11}, D-Nle⁸, Nle¹⁸, Tyr³⁴]hPTH-(1-34)NH₂, [D-Nle⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂ and [D-Bpa⁸, Tyr³⁴]hPTH(1-34)NH₂.

Please amend the paragraph beginning at page 20, line 3, as follows:

a8

A peptide of this invention is also denoted herein by another format, e.g., [D-Nle⁸]hPTH(1-34)NH₂, with the substituted amino acids from the natural sequence placed between the set of brackets (e.g., D-Nle⁸ for Met⁸ in hPTH). The abbreviation hPTH stands for human PTH, and hPTHrP for human PTHrP. The numbers between the parentheses refer to the number of amino acids present in the peptide (e.g., hPTH(1-34) is amino acids 1 through 34 of

a⁸ the peptide sequence for human PTH; SEQ ID NO:1). The sequences for hPTH(1-34) (SEQ ID NO:1) and hPTHrP(1-34) (SEQ ID NO:2) are listed in Nissenson, et al., Receptor, 3:193 (1993). The designation "NH₂" in PTH(1-34)NH₂ (SEQ ID NO:53) indicates that the C-terminus of the peptide is amidated. PTH(1-34) (SEQ ID NO:1) means that the C-terminus is the free acid.

Please amend the paragraph beginning at page 21, line 37, as follows:

a⁹ Receptor binding assay: Ligand binding is performed using Saos-2/B-10, HEK/C-21 cells or HEK/BP-16 cells using HPLC-purified [¹²⁵I][Nle^{8,18}, Tyr³⁴]bPTH-(1-34)NH₂ (¹²⁵I-PTH) (SEQ ID NO:17) as radioligand. Saos-2 cells are maintained for four days until they reach confluence. The medium is replaced with 5% FBS in RPMI 1640 medium and incubated for about 2 hrs at room temperature with 10 x 10⁴ cpm mono-¹²⁵I-[Nle^{8,18}, Tyr³⁴(3-¹²⁵I)]bPTH(1-34)NH₂ (SEQ ID NO:17) in the presence of competing peptides of the invention at various concentrations between 10⁻¹¹M to 10⁻⁴M. The cells are washed four times with ice-cold PBS and lysed with 0.1 M NaOH, and the radioactivity associated with the cells is counted in a scintillation counter. Synthesis of mono-¹²⁵I-[Nle^{8,18}, Tyr³⁴(3-¹²⁵I)]bPTH(1-34)NH₂ (SEQ ID NO:17) is carried out as described in Goldman, M.E., et al., Endocrinol., 123:1468 (1988).

Please amend the paragraph beginning at page 22, line 14, as follows:

a¹⁰ The binding assay is conducted with various peptides of the invention, and the K_d value (half maximal inhibition of binding of mono-¹²⁵I-[Nle^{8,18}, Tyr³⁴(3-¹²⁵I)]bPTH(1-34)NH₂ (SEQ ID NO:17)) for each peptide is calculated.

Please amend the table beginning at page 29, line 15, as follows:

a¹¹

Example	Name	Mass Spec.
3	[Cha ^{7,11} , des-Met ⁸ , Nle ¹⁸ , Tyr ³⁴]hPTH(1-34)NH ₂ (<u>SEQ ID NO:16</u>)	4063.5
4	[Cha ^{7,11} , D-Nle ⁸ , des-Met ¹⁸ , Tyr ³⁴]hPTH(1-34)NH ₂	4063.4
5	[D-Bpa ⁸ , Tyr ³⁴]hPTH-(1-34)NH ₂	4320.7

Please amend the paragraph beginning at page 29, line 21, as follows:

Examples 6 to 86 can be synthesized substantially according to the procedure of

Example 1 using the appropriate, protected amino acids.

Example 6: [D-Nle⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 7: [D-Nle⁸]hPTH(1-34)NH₂

Example 8: [D-Leu⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 9: [D-Cha⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 10: [D-Phe⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 11: [D-Nal⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 12: [D-Abu⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 13: [D-Met⁸]hPTH(1-34)NH₂

Example 14: [Cha^{7,11}, D-Met⁸]hPTH(1-34)NH₂

Example 15: [D-Ile⁸]hPTH(1-34)NH₂

Example 16: [Cha^{7,11}, D-Ile⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 17: [D-Ile⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 18: [D-Leu⁸]hPTH(1-34)NH₂

Example 19: [Cha^{7,11}, D-Leu⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 20: [D-Val⁸]hPTH(1-34)NH₂

Example 21: [Cha^{7,11}, D-Val⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 22: [D-Val⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 23: [D-Cha⁸]hPTH(1-34)NH₂

Example 24: [Cha^{7,11}, D-Cha⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 25: [D-Ala⁸]hPTH(1-34)NH₂

Example 26: [Cha^{7,11}, D-Ala⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 27: [D-Ala⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 28: [D-Phe⁸]hPTH(1-34)NH₂

Example 29: [Cha^{7,11}, D-Phe⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 30: [D-Met⁸]hPTH(7-34)NH₂

Example 31: [D-Nal⁸]hPTH(1-34)NH₂

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- Example 32: [D-Trp⁸]hPTH(1-34)NH₂
- Example 33: [Cha^{7,11}, D-Trp⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂
- Example 34: [D-Trp⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂
- Example 35: [D-Abu⁸]hPTH(1-34)NH₂
- Example 36: [Cha^{7,11}, D-Abu⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂
- Example 37: [des-Met⁸]hPTH(1-34)NH₂ (SEQ ID NO:18)
- Example 38: [Cha^{7,11}, des-Met⁸]hPTH(1-34)NH₂ (SEQ ID NO:19)
- Example 39: [Cha^{7,11}, des-Met⁸, des-Met¹⁸, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:20)
- Example 40: [des-Met⁸, des-Met¹⁸]hPTH(1-34)NH₂ (SEQ ID NO:21)
- Example 41: [Cha^{7,11}, des-Met⁸, des-Met¹⁸]hPTH(1-34)NH₂ (SEQ ID NO:22)
- Example 42: [des-Met⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:23)
- Example 43: [des-Met¹⁸]hPTH(1-34)NH₂ (SEQ ID NO:24)
- Example 44: [Cha^{7,11}, des-Met¹⁸]hPTH(1-34)NH₂ (SEQ ID NO:25)
- Example 45: [Cha^{7,11}, des-Met¹⁸, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:26)
- Example 46: [D-Nle⁸, des-Met¹⁸, Tyr³⁴]hPTH(1-34)NH₂
- Example 47: [des-Glu⁶Gln⁶, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:27)
- Example 48: [des-Leu⁷, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:28)
- Example 49: [des-His⁹, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:29)
- Example 50: [des-Asn¹⁰, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:30)
- Example 51: [des-Leu¹¹, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:31)
- Example 52: [des-Gly¹², Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:32)
- Example 53: [des-Lys¹³, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:33)
- Example 54: [des-His¹⁴, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:34)
- Example 55: [des-Leu¹⁵, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:35)
- Example 56: [des-Asn¹⁶, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:36)
- Example 57: [des-Ser¹⁷, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:37)
- Example 58: [des-Glu¹⁹, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:38)
- Example 59: [des-Arg²⁰, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:39)
- Example 60: [des-Val²¹, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:40)
- Example 61: [des-Glu²², Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:41)

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Example 62: [~~des-Leu~~⁶Gln⁶, Cha^{7,11}, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:42)

Example 63: [des-Leu⁷, Nle^{8,18}, Cha¹¹, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:43)

Example 64: [Cha^{7,11}, des-His⁹, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂ (SEQ ID NO:44)

Example 65: [~~des-Leu~~⁶Gln⁶, Cha^{7,11}, D-Nle⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 66: [des-Leu⁷, D-Nle⁸, Cha¹¹, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 67: [Cha^{7,11}, D-Nle⁸, des-His⁹, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 68: [Cha^{7,11}, des-Met⁸, des-His⁹, des-Asn¹⁰]hPTH(1-34)NH₂ (SEQ ID NO:45)

Example 69: [Cha^{7,11}, des-Ser¹⁷, des-Met¹⁸, des-Glu¹⁹]hPTH(1-34)NH₂ (SEQ ID NO:46)

Example 70: [D-Met⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 71: [D-Met⁸, Tyr³⁴]hPTH(1-34)NH₂

Example 72: [D-Nle⁸, Nle¹⁸, Tyr³⁴]hPTH(7-34)NH₂

Example 73: [D-Nle⁸, Nle¹⁸]hPTH(7-34)NH₂

Example 74: [Ile⁵, D-Leu⁸]hPTHrP(1-34)NH₂

Example 75: [Ile⁵, D-Leu⁸, Trp²³]hPTHrP(1-34)NH₂

Example 76: [Ile⁵, des-Leu⁸, Trp²³]hPTHrP(1-34)NH₂ (SEQ ID NO:47)

Example 77: [Ile⁵, des-Leu⁸]hPTHrP(1-34)NH₂ (SEQ ID NO:48)

Example 78: [des-Leu⁸, Trp²³]hPTHrP(1-34)NH₂ (SEQ ID NO:49)

Example 79: [Ile⁵, des-Leu¹⁸]hPTHrP(1-34)NH₂ (SEQ ID NO:50)

Example 80: [Ile⁵, des-Leu¹⁸, Trp²³]hPTHrP(1-34)NH₂ (SEQ ID NO:51)

Example 81: [des-Leu¹⁸, Trp²³]hPTHrP(1-34)NH₂ (SEQ ID NO:52)

Example 82: [Ile⁵, D-Leu⁸, Glu^{22,25}, Leu^{23,28,31}, Lys^{26,30}, Aib²⁹]hPTHrP(1-34)NH₂

Example 83: [Ile⁵, D-Leu⁸, Glu^{22,25}, Trp²³, Lys^{26,30}, Leu^{28,31}, Aib²⁹]hPTHrP(1-34)NH₂

Example 84: [Ile⁵, D-Leu⁸, Glu^{22,25,29}, Leu^{23,28,31}, Lys^{26,30}]hPTHrP(1-34)NH₂

Example 85: [Ile⁵, D-Leu⁸, Glu^{22,25,29}, Trp²³, Lys^{26,30}, Leu^{28,31}]hPTHrP(1-34)NH₂

Example 86: [D-Leu⁸, Trp²³]hPTHrP(7-34)NH₂
